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25 October, 2004

BY FAX

Our ref: ITT0055

The International Bureau of WIPO
34 chemin des Colombettes
1211 Geneva 20
SWITZERLAND

Dear Sirs,

**PCT Application No. PCT/GB2004/001437 in the name of**
**Istituto di Ricerche di Biologia Molecolare P. Angeletti SPA et al**

I am writing in response to the Written Opinion of the International Searching Authority pursuant to PCT Rule 43 bis. 1 dated 26 July 2004.

Amendments under Article 19 PCT

Please find enclosed replacement pages 105, 106 and 120 to 122 to replace pages 105, 106 and 120 currently on file. For the convenience of the IB, manuscript-amended pages are also enclosed.

Specifically, Claim 1 has been amended to correct some minor typographical errors in the definitions of $Q^1$ and $R^{13}$. On page 105, line 13, the term "-O-$(CH_2)_{2-4}R^cR^d$" has been corrected to read "-O-$(CH_2)_{2-4}NR^cR^d$"; an example of such a substituent may be found on page 101, (last example) of the description. On page 105, line 14, the term "-O-$CR^eR^f$" has been corrected to read "-O-$CHR^eR^f$"; an example of such a substituent may be found on page 95 (first example) of the description. On page 106, line 29, the term "$C_{3-8}$ heteroalkyl" has been corrected to read "$C_{3-8}$ cycloalkyl".

Furthermore, Claim 8 has been amended to clarify the reaction steps. Basis for this amendment may be found in the description on pages 23 to 25.

For the avoidance of doubt, Claims 2 to 7 are unchanged.

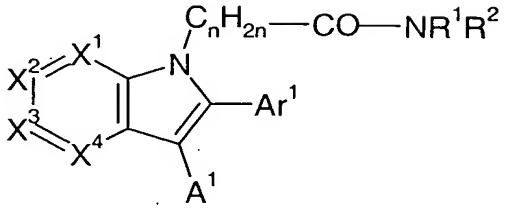
Yours faithfully,

Jocelyn Man
European Patent Attorney

Encs. Replacement pages 105, 106 and 120 to 122;
Manuscript-amended pages 105, 106 and 120.

## CLAIMS

1. A compound of formula (I):



(I)

wherein

$Ar^1$ is a moiety containing at least one aromatic ring and possesses 5-, 6-, 9- or 10-ring atoms optionally containing 1, 2 or 3 heteroatoms independently selected from N, O and S, which ring is optionally substituted at any substitutable position by groups $Q^1$ and $Q^2$;

$Q^1$ is halogen, hydroxy, $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, aryl, heteroaryl, $CONR^cR^d$, $C_mH_{2m}NR^cR^d$, $-O-(CH_2)_{2-4}NR^cR^d$, $-O-C_mH_{2m}CONR^cR^d$, $-O-C_mH_{2m}$ aryl, $-O-C_mH_{2m}$ heteroaryl, $-O-CHR^eR^f$;

$R^c$ and $R^d$ are each independently selected from hydrogen, $C_{1-4}$ alkyl and $C(O)C_{1-4}$ alkyl;

or $R^c$, $R^d$ and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7 ring atoms, where said ring is optionally substituted by halogen, hydroxy, $C_{1-4}$ alkyl or $C_{1-4}$ alkoxy;

m is 0, 1, 2 or 3

$R^e$ and $R^f$ are each independently selected from hydrogen and $C_{1-4}$ alkoxy;

or $R^e$ and $R^f$ are linked by a heteroatom selected from N, O and S to form a heteroaliphatic ring of 4 to 7 ring atoms, where said ring is optionally substituted by halogen, hydroxy, $C_{1-4}$ alkyl or $C_{1-4}$alkoxy;

and wherein said $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy and aryl groups are optionally substituted by halogen or hydroxy;

$Q^2$ is halogen, hydroxy, $C_{1-4}$ alkyl or $C_{1-4}$ alkoxy, where said $C_{1-4}$ alkyl and $C_{1-4}$ alkoxy groups are optionally substituted by halogen or hydroxyl;

or $Q^1$ and $Q^2$ may be linked by a bond or a heteroatom selected from N, O and S to form a ring of 4 to 7 atoms, where said ring is optionally substituted by halogen, hydroxy, $C_{1-4}$ alkyl or $C_{1-4}$ alkoxy;

$A^1$ is $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, where said $C_{1-6}$ alkyl and $C_{2-6}$ alkenyl groups are optionally substituted by $C_{1-4}$ alkoxy or up to 5 fluorine atoms, or a non-aromatic ring of 3 to 8 ring atoms where said ring may contain a double bond and/or may contain a O, S, SO, $SO_2$ or NH moiety and where said ring is optionally substituted by one or two alkyl groups of up to 2 carbon atoms or by 1 to 8 fluorine atoms, or a non-aromatic bicyclic moiety of 4 to 8 ring atoms which ring may be optionally substituted by fluorine or hydroxy;

$X^1$ is N or $CR^a$;

$X^2$ is N or $CR^3$;

$X^3$ is N or $CR^4$;

$X^4$ is N or $CR^b$;

with the proviso that $X^2$ and $X^3$ are not both N;

$R^a$ and $R^b$ are each independently selected from hydrogen, fluorine, chlorine, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl or $C_{1-4}$ alkoxy, where said $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl and $C_{1-4}$ alkoxy groups are optionally substituted by hydroxy or fluorine;

one of $R^3$ or $R^4$ is hydrogen, halogen, $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, CN, $CO_2H$, $CO_2C_{1-4}$ alkyl, aryl, heteroaryl or $C(O)NR^9R^{10}$, where said $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, aryl and heteroaryl groups are optionally substituted by hydroxy or fluorine;

$R^9$ is hydrogen or $C_{1-4}$ alkyl;

$R^{10}$ is hydrogen, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl or $(CH_2)_{0-3}R^{12}$ or $SO_2R^{11}$;

$R^{12}$ is $NR^hR^i$, $OR^h$, aryl, heteroaryl, indolyl or Het;

$R^h$ and $R^i$ are each independently selected from hydrogen and $C_{1-4}$ alkyl;

Het is a heteroaliphatic ring of 4 to 7 ring atoms, which ring may contain 1, 2 or 3 heteroatoms selected from N, O or S or a group S(O), $S(O)_2$, NH or $NC_{1-4}$ alkyl;

$R^{11}$ is $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl or $(CH_2)_{0-3}R^{13}$;

$R^{13}$ is aryl, heteroaryl, $C_{1-4}$ alkyl, $C_{3-8}$ cycloalkyl, Het or $NR^mR^n$, wherein Het is as hereinbefore defined, $R^m$ and $R^n$ are each independently selected from hydrogen, $C_{1-4}$ alkyl and $CO_2(CH_2)_{0-3}$aryl, and wherein $R^{13}$ is optionally substituted by halogen, $C_{1-4}$ alkyl or $NR^oR^p$, wherein $R^o$ and $R^p$ are each independently selected from hydrogen and $C_{1-4}$ alkyl;

3-cyclohexyl-1-[2-(dimethylamino)-2-oxoethyl]-2-phenyl-N-(pyridin-3-ylsulfonyl)-1H-indole-6-carboxamide,
3-cyclohexyl-1-[2-(dimethylamino)-2-oxoethyl]-2-phenyl-N-(3-thienylsulfonyl)-1H-indole-6-carboxamide,
or a pharmaceutically acceptable salt thereof.

4. A compound as claimed in any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof for use in therapy.

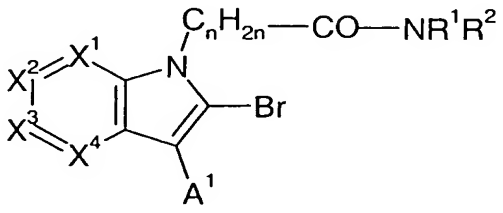
5. A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable carrier.

6. A method for the treatment or prevention of illness due to hepatitis C virus, which method comprises administration to a subject suffering from the condition a compound as claimed in any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof.

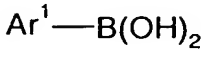
7. Use of a compound as claimed in any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus.

8. A process for the preparation of a compound as claimed in any one of claims 1 to 3 which comprises: either

(A) reacting a compound of formula (II) with a compound of formula (III):



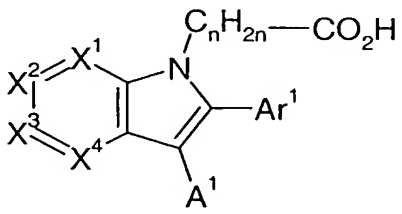
(II)



(III)

wherein $X^1$, $X^2$, $X^3$, $X^4$, $R^1$, $R^2$, $A^1$ and $Ar^1$ are as defined in Claim 1, in the presence of a Pd(0) catalyst under conditions typical for the Suzuki reaction;

(B) reacting a compound of formula (IV) with a compound of formula (V):



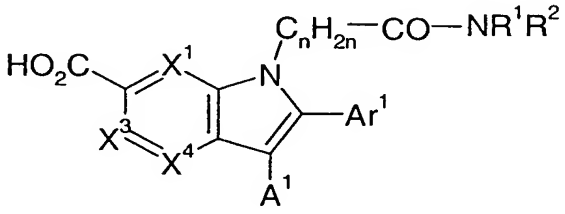
(IV)

$HNR^1R^2$

(V)

wherein $X^1$, $X^2$, $X^3$, $X^4$, $A^1$, $Ar^1$, n, $R^1$ and $R^2$ are as defined in Claim 1, in the presence of a coupling reagent and a base;

(C) where $X^2$ is $CR^3$ and $R^3$ is $C(O)NR^9R^{10}$, reacting a compound of formula (VI) with a compound of formula (VII):



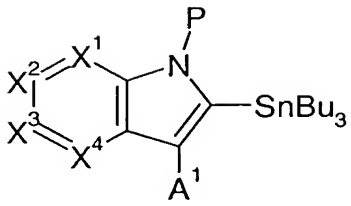
(VI)

$HNR^9R^{10}$

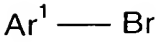
(VII)

wherein $X^1$, $X^3$, $X^4$, $A^1$, $Ar^1$, n, $R^1$, $R^2$, $R^9$ and $R^{10}$ are as defined in Claim 1, essentially in the same manner as general process (B);

(D) where the (aza)indolyl nitrogen atom is suitably protected, reacting a compound of formula (VIII) with a compound of formula (IX):



(VIII)



(IX)

where P is a suitable protecting group and wherein $X^1$, $X^2$, $X^3$, $X^4$, $A^1$ and $Ar^1$ are as defined in Claim 1, effected in the presence of a Pd(0) catalyst, a suitable ligand and a salt in a suitable solvent at a temperature between 20°C and the reflux temperature of the solvent; or

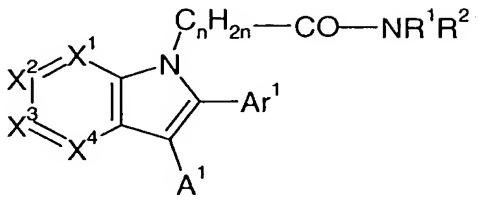
(E) where $X^2$ is $CR^3$ and $R^3$ is $C(O)NR^9R^{10}$ and $R^9$ is $SO_2R^{11}$, reacting a compound of formula (VI) with a compound of formula (X):

$$R^{11}O_2S\text{-}NHR^{10} \qquad (X)$$

wherein $X^1$, $X^3$, $X^4$, $A^1$, $Ar^1$, n, $R^1$, $R^2$, $R^{10}$ and $R^{11}$ are as defined in Claim 1, in the presence of an activator and/or a dehydrating agent in a suitable solvent.

## CLAIMS

1. A compound of formula (I):



(I)

wherein

$Ar^1$ is a moiety containing at least one aromatic ring and possesses 5-, 6-, 9- or 10-ring atoms optionally containing 1, 2 or 3 heteroatoms independently selected from N, O and S, which ring is optionally substituted at any substitutable position by groups $Q^1$ and $Q^2$;

$Q^1$ is halogen, hydroxy, $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, aryl, heteroaryl, $CONR^cR^d$, $C_mH_{2m}NR^cR^d$, $-O-(CH_2)_{2-4}NR^cR^d$, $-O-C_mH_{2m}CONR^cR^d$, $-O-C_mH_{2m}$ aryl, $-O-C_mH_{2m}$ heteroaryl, $-O-CHR^eR^f$;

$R^c$ and $R^d$ are each independently selected from hydrogen, $C_{1-4}$ alkyl and $C(O)C_{1-4}$ alkyl;

or $R^c$, $R^d$ and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7 ring atoms, where said ring is optionally substituted by halogen, hydroxy, $C_{1-4}$ alkyl or $C_{1-4}$ alkoxy;

m is 0, 1, 2 or 3

$R^e$ and $R^f$ are each independently selected from hydrogen and $C_{1-4}$ alkoxy;

or $R^e$ and $R^f$ are linked by a heteroatom selected from N, O and S to form a heteroaliphatic ring of 4 to 7 ring atoms, where said ring is optionally substituted by halogen, hydroxy, $C_{1-4}$ alkyl or $C_{1-4}$alkoxy;

and wherein said $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy and aryl groups are optionally substituted by halogen or hydroxy;

$Q^2$ is halogen, hydroxy, $C_{1-4}$ alkyl or $C_{1-4}$ alkoxy, where said $C_{1-4}$ alkyl and $C_{1-4}$ alkoxy groups are optionally substituted by halogen or hydroxyl;

or $Q^1$ and $Q^2$ may be linked by a bond or a heteroatom selected from N, O and S to form a ring of 4 to 7 atoms, where said ring is optionally substituted by halogen, hydroxy, $C_{1-4}$ alkyl or $C_{1-4}$ alkoxy;

$A^1$ is $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, where said $C_{1-6}$ alkyl and $C_{2-6}$ alkenyl groups are optionally substituted by $C_{1-4}$ alkoxy or up to 5 fluorine atoms, or a non-aromatic ring of 3 to 8 ring atoms where said ring may contain a double bond and/or may contain a O, S, SO, $SO_2$ or NH moiety and where said ring is optionally substituted by one or two alkyl groups of up to 2 carbon atoms or by 1 to 8 fluorine atoms, or a non-aromatic bicyclic moiety of 4 to 8 ring atoms which ring may be optionally substituted by fluorine or hydroxy;

$X^1$ is N or $CR^a$;

$X^2$ is N or $CR^3$;

$X^3$ is N or $CR^4$;

$X^4$ is N or $CR^b$;

with the proviso that $X^2$ and $X^3$ are not both N;

$R^a$ and $R^b$ are each independently selected from hydrogen, fluorine, chlorine, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl or $C_{1-4}$ alkoxy, where said $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl and $C_{1-4}$ alkoxy groups are optionally substituted by hydroxy or fluorine;

one of $R^3$ or $R^4$ is hydrogen, halogen, $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, CN, $CO_2H$, $CO_2C_{1-4}$ alkyl, aryl, heteroaryl or $C(O)NR^9R^{10}$, where said $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, aryl and heteroaryl groups are optionally substituted by hydroxy or fluorine;

$R^9$ is hydrogen or $C_{1-4}$ alkyl;

$R^{10}$ is hydrogen, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl or $(CH_2)_{0-3}R^{12}$ or $SO_2R^{11}$;

$R^{12}$ is $NR^hR^i$, $OR^h$, aryl, heteroaryl, indolyl or Het;

$R^h$ and $R^i$ are each independently selected from hydrogen and $C_{1-4}$ alkyl;

Het is a heteroaliphatic ring of 4 to 7 ring atoms, which ring may contain 1, 2 or 3 heteroatoms selected from N, O or S or a group S(O), $S(O)_2$, NH or $NC_{1-4}$ alkyl;

$R^{11}$ is $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl or $(CH_2)_{0-3}R^{13}$;

$R^{13}$ is aryl, heteroaryl, $C_{1-4}$ alkyl, $C_{3-8}$ ~~hetero~~cycl alkyl, Het or $NR^mR^n$, wherein Het is as hereinbefore defined, $R^m$ and $R^n$ are each independently selected from hydrogen, $C_{1-4}$ alkyl and $CO_2(CH_2)_{0-3}$aryl, and wherein $R^{13}$ is optionally substituted by halogen, $C_{1-4}$ alkyl or $NR^oR^p$, wherein $R^o$ and $R^p$ are each independently selected from hydrogen and $C_{1-4}$ alkyl;

3-cyclohexyl-1-[2-(dimethylamino)-2-oxoethyl]-2-phenyl-N-(pyridin-3-ylsulfonyl)-1H-indole-6-carboxamide,
3-cyclohexyl-1-[2-(dimethylamino)-2-oxoethyl]-2-phenyl-N-(3-thienylsulfonyl)-1H-indole-6-carboxamide,
or a pharmaceutically acceptable salt thereof.

4. A compound as claimed in any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof for use in therapy.

5. A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable carrier.

6. A method for the treatment or prevention of illness due to hepatitis C virus, which method comprises administration to a subject suffering from the condition a compound as claimed in any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof.

7. Use of a compound as claimed in any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment or prevention of infection by hepatitis C virus.

8. A process for the preparation of a compound as claimed in any one of claims 1 to 3 which comprises <see replacement pages>